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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,855	02/27/2002	Evan C. Unger	UNGR-1632	8641

7590 01/09/2004

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	11

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,855	UNGER, EVAN C.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/27/02, 10/1/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 47-59* is/are pending in the application.

4a) Of the above claim(s) *48,52-54 and 56-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,47,49-51 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4-7*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1, 47-59 are pending

Election/Restrictions

Applicant's election of the species in which the lipid is a combination of at least one phosphatidylcholine, at least one phosphatidylethanolamine, and at least one phosphatidic acid; the gas is perfluorocarbon gas and the oil is triacetin in Paper No. 10 is acknowledged. Claims 1, 47, 49-51, 55 read on the elected species. Accordingly, the claims are searched and examined at least to the extent that they read on the elected species until an allowable subject matter is found. The examination may then be extended to other patentably distinct species.

Claims 48, 52-54, 56-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 47, 49-51, 55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-102 of U.S. Patent No. 6,146,657, claims 111-173 of U.S. Patent No. 6,139,819, claim 95 of US Patent No. 6,071,494, claims 57-122 of U.S. Patent 6,414,139 ('139). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the patented claims are directed to compositions comprising gaseous liposomes, a bioactive agent, and a surfactant, wherein the gas is a perfluorocarbon.

For example, claims 57-122 of the US '139 are directed to compositions comprising a gaseous vesicle (claims 57, 60-64), a bioactive agent (claim 82) wherein the gas is a perfluorocarbon. The cited patents only lack to specifically claim an oil with their compositions. However, it would have been obvious to one of ordinary skill in the art at the time of invention to further add suitable oil into the compositions of the patented claims, because employing an oil to improve solubility of bioactive agents is well recognized practice in the art of pharmaceutical formulation. Accordingly, the ordinary skill in the art would have been able to practice the instant claims when in possession of the patented claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 47, 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Grinstaff et al US Patent 5,498,421.

The instant claims are directed to compositions comprising a therapeutic agent, a lipid microsphere encapsulating a perfluorocarbon gas and an oil.

Grinstaff discloses compositions comprising a biologic agent, a polymeric shell encapsulating a perfluorocarbon gas and an oil. (abstract, col 12, lines 10-40, examples 13, 35-37, 40, 46, claim 1, 12-13). The polymeric shell of Grinstaff is modified phospholipids which meets the limitation of the instant recitation "stabilized lipid microsphere." (see claim 26). Thus, Grinstaff meets the limitations of the instant compositions.

Claims 1, 47, 51 are rejected under 35 U.S.C. 102(e) as being anticipated by Lanza et al US Patent 5,989,520

Lanza discloses targeted therapeutic emulsions having a lipid wall which is a phospholipid (abstract; col 5 lines 51-65; col 6 lines 45-50), a gas therein such as perfluorinated compounds in combination with an oil (col 5, line 50-col 6, line 55; col 7, line 3; col 8, lines 18-49) and a therapeutic agent or drugs for a desired sites (col 4, lines 45-56; col 5, lines 20-30). Lanza et al further indicate their particles may be used for delivery of drugs to desired sites while the progress of the treatment may be monitored through repeated imaging at such sites (col 4, lines 47-55). Lanza meets all the elements of the instant generic claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 47, 51, 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza in view of Klaveness US Patent 6,261,537.

The teachings of Lanza are described above. Lanza fails to use a triacetin in his compositions.

Klaveness teaches the use of triacetin (see col 59, line 25). Klaveness further discloses targeted compositions comprising phospholipid-stabilized gas microbubbles, and a therapeutic agent. The gas of Klaveness can be a fluorocarbon. (see col 117, lines 1-30; col 118, lines 20-30).

The teachings of Lanza and Klaveness are in the same field of endeavor because they are both directed to targeted gaseous compositions for therapeutic use.

Accordingly, even though Lanza does not specifically employ triacetin, it would have been obvious to one of ordinary skill in the art at the time of invention to use triacetin in place of the therapeutic agent of Lanza, because as suggested by Klaveness, the ordinary skill in the art would have had a reasonable expectation of success in delivering any such agents as taught by Klaveness into the target cells.

Claims 1, 47, 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza in view of Unger et al US Patent 5,469,854.

The teachings of Lanza are described above. Lanza specifically suggest the use of lipid walls comprising suitable phospholipid moieties. (col 6, lines 25-40). Lanza fails to explicitly use a lipid wall comprising at least one phosphatidylcholine, at least one phosphatidylethanolamine, and at least one phosphatidic acid.

Unger teaches gas-filled lipid microspheres comprising at least one phosphatidylcholine, at least one phosphatidylethanolamine, and at least one phosphatidic acid that possess good acoustic window. (see abstract; claims 1, 15-16).

Lanza and Unger are in the same field of endeavor because they both teach gas containing targeted drug delivery systems for therapeutic use.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the lipid wall composition of Lanza with those suggested by Unger, because as suggested by Unger, the ordinary skill in the art would have had a reasonable expectation of success to improves the integrity and acoustic behavior of lipid microspheres when using a combination of least one phosphatidylcholine, at least one phosphatidylethanolamine, and at least one phosphatidic acid as the wall material.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

RUSSELL TRAVERS
PRIMARY EXAMINER

SS 12/22/03